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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/483,672	01/14/2000	Jiangchun Xu	210121.42711C11	8685

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EXAMINER	
MORAN, MARJORIE A	
ART UNIT	**PAPER NUMBER**
1631	20

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/483,672	Applicant(s) XU ET AL.	
	Examiner Marjorie A. Moran	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 March 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4-18,21-65 and 72-79* is/are pending in the application.

4a) Of the above claim(s) *4-18 and 23-64* is/are withdrawn from consideration.

5)☒ Claim(s) *65 and 74* is/are allowed.

6)☒ Claim(s) *21,22,72,73 and 75-79* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *15,16,17* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

All rejections and objections not repeated below are hereby withdrawn. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Claims 4-18 and 23-64 are again withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 12.

This application contains claims 4-18 and 23-64 drawn to an invention nonelected without traverse in Paper No. 12. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

New claims 73-79 are drawn to the same subject matter as the claims of originally elected Group I, and are therefore also considered elected.

An action on the merits of claims 21-22, 65, and 72-79, as they read on elected SEQ ID NO: 525, follows.

Information Disclosure Statement

The IDS's filed 12/31/01 (paper #15), 10/17/01 (paper #16) and 5/13/02 (paper #17) have all been considered in full.

Drawings

It is noted that a response containing corrected drawings was originally filed 3/6/02 and stamped as received in OIPE on 3/18/02. As the originally filed response was not received by

the examiner, the attorney kindly sent a copy of all originally filed papers by FAX. Unfortunately, all the papers, including drawings, were received with a horizontal line through the middle of each page. The examiner thanks the applicants and attorney for their forbearance, and requests that another copy of the corrected drawings be filed for review by the draftsperson. To facilitate further examination, applicant is requested to file new copies of the corrected drawings within the time period for response to this office action.

Priority

Applicant is reminded that priority for claims reciting SEQ ID NO: 525 is granted only to 11/12/99.

Claim Rejections - 35 USC § 112

Claims 73, 75, and 77-79 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a NEW MATTER rejection.

Compositions comprising a polypeptide comprising amino acids 1-39 of SEQ ID NO: 525, or comprising polypeptides with at least 90% identity of a polypeptide comprising amino acids 1-39 of SEQ ID NO: 525 are new matter.

Applicant's attention is directed to MPEP 2163.05, which states: "The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571,

39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967)."

The specification teaches SEQ ID NO: 525, which is 254 amino acids long. The specification further discloses, on page 27, that polynucleotides comprise at least 15, 30, or 45 consecutive residues, which would result in polypeptides of at least 3, 10, or 15 amino acids. Similarly, the specification discloses on page 3 that polynucleotides may encode portions of a polypeptide comprising 15 amino acids. Nowhere does the specification describe a polypeptide comprising 39 amino acids nor a polynucleotide encoding a polypeptide comprising 39 amino acids, specifically residues 1-39 of SEQ ID NO: 525. The specification does not disclose fragments of any polypeptide comprising specific amino acid residues, nor any fragments comprising 39 amino acids. Originally filed claims 1-3 recited polypeptides and complements thereof, and claim 4 recites a polynucleotide encoding a polypeptide of at least 15 amino acids, but none of the originally filed claims recites a polypeptide comprising 39 amino acids, specifically a polypeptide comprising residues 1-39 of SEQ ID NO: 525. The specification therefore provides support for the entirety (genus) of SEQ ID NO: 525, but does not provide support for the fragment (species) recited in claims 73 and 75. As neither the originally filed specification or claims teach or recite a polypeptide comprising residues 1-39 of SEQ ID NO: 525, or for a polypeptide with 90% identity to a polypeptide comprising residues 1-39 of SEQ ID NO: 525, the claims are rejected as reciting new matter.

Claims 73 and 75 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one

skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 77-79 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising SEQ ID NO: 525, and polypeptides with 90% or 95% identity thereto, which contain an amino acid sequence capable of stimulating human T-cells, does not reasonably provide enablement for compositions comprising a polypeptide comprising residues 1-39 of SEQ ID NO: 525, and polypeptides 90% identical thereto, which contain an amino acid sequence capable of stimulating human T-cells . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining what constitutes undue experimentation were affirmed by the court in *In re Wands* (8 USPQ2d 1400 (CAFC 1986)). These factors are the quantity of experimentation; the amount of direction or guidance presented in the specification; the presence or absence of working examples; the nature of the invention; the state of the prior art; the level of skill of those in the art; predictability or unpredictability of the art; and the breadth of the claims.

Compositions comprising SEQ ID NO: 525, and polypeptides with 90% or 95% identity thereto, which contain an amino acid sequence capable of stimulating human T-cells are enabled by the teaching of the specification, but compositions comprising a polypeptide comprising residues 1-39 of SEQ ID NO: 525, and polypeptides 90% identical thereto, which contain an amino acid sequence capable of stimulating human T-cells are not enabled because neither the specification nor the prior art teaches any portion of such a polypeptide which is known to be capable of stimulating T-cells.

The specification teaches, on page that SEQ ID NO: 338, a 9-mer peptide, is a naturally processed epitope from clone P703P which is capable of stimulating T-cells. The

specification further discloses, on pages 25 and 77 that SEQ ID NO: 524 is the full-length cDNA of P703P, and that SEQ ID NO: 524 encodes SEQ ID NO: 525. The 9-mer represented by SEQ ID NO: 338 corresponds to residues 112-120 of SEQ ID NO: 525, therefore one skilled in the art would reasonable conclude that a polypeptide comprising residues 112-120 of SEQ ID NO: 525 would be a polypeptide comprising an amino acid sequence capable of stimulating human T-cells. The state of the prior art is such that it is well known that epitopes from a polypeptide must interact with T-cell receptors or be presented on the surface of antigen-presenting cells in order to stimulate T-cells. While it is known that size is a factor in processing an recognition of an epitope, it is also known that other factors are involved in T-cell stimulation, all of which have not been elucidated. For support, see BIXLER et al. (US 5,785,973, col. 5, line 47-col. 7, line 59). The prior art of GEYSEN (US 5,539,084) shows that even for peptides of similar size derived from the same "parent" polypeptide, not all will be capable of interacting with T-cells (col. 2, lines 5-9 and Figure 6), thus demonstrating the degree of uncertainty in the art for predicting which subsets or fragments of a larger polypeptide will be capable of interacting with, or stimulating T-cells. Neither the specification nor the prior art teach any portion of SEQ ID NO: 525, other than residues 112-120, which is known to be capable of stimulating T-cells. The level of skill in the art is acknowledged to be high; however, due to the high degree of uncertainty in predicting what fragments of a polypeptide would be expected to be capable of stimulating T-cells, and the lack of teaching in either the specification or the prior art that a polypeptide comprising residues 1-39 of SEQ ID NO: 525 is known to be capable of stimulating T-cells, it would require undue experimentation by one skilled in the art to determine if a polypeptide comprising residues 1-39 of SEQ ID NO: 525 can stimulate human T-cells. For the reasons set forth above, claims 73 and 75 are not enabled, and claims 77-79 are not enabled where they depend from claims 73 and 75.

Claim Rejections - 35 USC § 102

Claims 21, 72 and 76 are rejected under 35 U.S.C. 102(e) as being anticipated by GIMENO et al. (US 5,955,306).

GIMENO teaches a protein represented by his SEQ ID NO: 31 (col's 73-76), which is 97.6% identical to instant SEQ ID NO: 525. The specification discloses on page 88 that a 9-mer corresponding to amino acids 112-120 of instant SEQ ID NO: 525 is a "naturally processed epitope" that can be used to stimulate T-cells. As a property is inherent to a product, any sequence comprising this 9-mer would be expected to be capable of stimulating T-cells. Residues 82-90 of GIMENO's sequence are identical to residues 112-120 of instant SEQ ID NO: 525, therefore GIMENO's sequence comprises an amino acid sequence capable of stimulating human T-cells, and claims 72 and 76 are anticipated. GIMENO teaches that his proteins are immunogenic (col. 29, lines 33-44) and may be mixed with an adjuvant for administration (col. 29, lines 47-48), thereby anticipating claim 21.

Applicant's arguments filed 3/6/02 have been fully considered but they are not persuasive. Applicant argues that the claims recite a polypeptide with at least 90% identity to the entirety of SEQ ID NO: 525. In response, applicant's attention is directed to the fact that GIMENO's sequence is 97.6% (i.e. more than 95%) identical to the entirety of SEQ ID NO: 525. Arguments with regard to a polypeptide with identity to a sequence comprising amino acids 1-39 of SEQ ID NO: 525 are moot as claims reciting such a limitation are not rejected herein. As GIMENO's sequence is at least 95% identical to SEQ IDNO: 525, and comprises an amino acid sequence expected to be capable of stimulating T-cells, the examiner maintains that GIMENO anticipates the claims. For these reasons, the rejection of claims 21 and 72 is maintained and new claim 76 is rejected.

Claim Rejections - 35 USC § 103

Claims 21-22, 72, and 76-77 are rejected under 35 U.S.C. 103(a) as being unpatentable over GIMENO et al. (US 5,955,306) in view of HAUSER et al. (US 5,776,468).

Claim 72 recites a composition comprising an immunostimulant and an isolated polypeptide comprising a sequence with at least 90% identity to the entirety of SEQ ID NO: 525, wherein the polypeptide comprises an amino acid sequence capable of stimulating human T-cells. Claim 76 limits the polypeptide to one with at least 95% identity to SEQ ID NO: 525. Claim 21 limits the immunostimulant to an adjuvant. Claim 22 limits the immunostimulant to one which elicits a Type I response. Claim 77 limits the immunostimulant to monophosphoryl lipid A (MPL), a CpG-containing oligonucleotide, a saponins, or a combination of these.

GIMENO teaches a peptide which is 97.6% identical to SEQ ID NO: 525, is immunogenic and may be formulated in a composition with an adjuvant or physiologically acceptable carrier, as set forth above. GIMENO does not teach an immunostimulant which induces a Type I response.

HAUSER teaches an improved adjuvant, small MPL, which preferentially induces IgG_{2a}, and induces a Type I response (col. 18, lines 5-30 and col. 28, lines 1-10).

It would have been obvious to one skilled in the art at the time of invention to have used HAUSER's MPL as an adjuvant in the composition of GIMENO where the motivation would have been to use an improved adjuvant, and to induce production of specific (desired) antibodies, such as IgG_{2a}, as suggested by HAUSER's teachings that MPL is an improved adjuvant compared to other known adjuvants, and his teaching that MPL specifically induces IgG_{2a} production.

Applicant's arguments filed 3/6/02 have been fully considered but they are not persuasive. In response to applicant's arguments that GIMENO does not teach the claimed polypeptides, and that HAUSER does not remedy the deficiencies of GIMENO, the examiner maintains, as set forth above, that GIMENO does teach the claimed polypeptides, and therefore maintains that GIMENO and HAUSER make obvious the claims for the reasons and motivations previously set forth and reiterated above.

Claims 21-22, 72, and 76-79 are rejected under 35 U.S.C. 103(a) as being unpatentable over GIMENO et al. (US 5,955,306) in view of CABEZON SILVA et al. (WO 9701640).

Claim 72 recites a composition comprising an immunostimulant and an isolated polypeptide comprising a sequence with at least 90% identity to the entirety of SEQ ID NO: 525, wherein the polypeptide comprises an amino acid sequence capable of stimulating human T-cells. Claim 76 limits the polypeptide to one with at least 95% identity to SEQ ID NO: 525. Claim 21 limits the immunostimulant to an adjuvant. Claim 22 limits the immunostimulant to one which elicits a Type I response. Claim 77 limits the immunostimulant to monophosphoryl lipid A (MPL), a CpG-containing oligonucleotide, a saponins, or a combination of these. Claim 78 limits the immunostimulant to 3D-MPL, QS21, or a combination thereof. Claim 79 limits the immunostimulant to comprise 3D-MPL, QS21 and tocopherol in an oil-in-water emulsion.

GIMENO teaches a peptide which is 97.6% identical to SEQ ID NO: 525, is immunogenic and may be formulated in a composition with an adjuvant or physiologically acceptable carrier, as set forth above. GIMENO does not teach the an immunostimulant which elicits a Type response nor the specific immunostimulants recited in the claims.

CABEZON SILVA teaches an adjuvant comprising QS21 and 3D-MPL in an oil-in-water emulsion comprising tocopherol (p. 6, lines 5-12) , teaches that this adjuvant elicits a TH1

response (p. 5, lines 16-19), and teaches that the combination of QSL and 3D-MPL in an oil-in-water emulsion is an improvement over other adjuvants because it induces a wider spectrum of immune responses to an antigen (p. 5, lines 28-34).

It would have been obvious to one of ordinary skill in the art at the time of invention to have used the QSL/3d_MPL/tocopherol oil-in-water emulsion of CABEZON SILVA as the adjuvant in the composition of GIMANO where the motivation would have been to elicit a better response to the polypeptide antigen, as suggested by the teaching of CABEZON SILVA that her adjuvant elicits a wider spectrum of response than other adjuvants.

Allowable Subject Matter

The following is a statement of reasons for the indication of allowable subject matter: The prior art neither teaches nor fairly suggests an isolated polypeptide comprising SEQ ID NO: 525, as recited in claims 65 and 74. As the entirety of SEQ ID NO: 525 comprises a 9-mer known to be capable of stimulating T-cells, as set forth above, claim 74 is enabled.

Conclusion

Claims 65 and 74 are allowed; claims 21-22, 72-73, and 75-79 are rejected. Claims 4-18 and 23-64 are again withdrawn.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marjorie A. Moran whose telephone number is (703) 305-2363. The examiner can normally be reached on Monday to Friday, 7:30 am to 4 pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward can be reached on (703) 308-4028. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 872-9306 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-3524.

MARJORIE MORAN
PATENT EXAMINER

November 14, 2002